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The Role of Chitinases in Atopic Dermatitis

Atopik Dermatitte Kitinazların Rolü

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Objectives: In this study, we investigated the acidic mammalian chitinase (AMCase) gene expression in skin biopsy samples taken from patients with atopic dermatitis.

Patients and methods: Five adult patients with atopic dermatitis were enrolled in this study between May 2005 and May 2007. Skin biopsy samples were taken from lesional and unaffected areas. AMCase gene expression was tested by real-time polymerase chain reaction. The AMCase gene products were compared with beta-actin.

Results: The AMCase production was higher in healthy regions of skin compared to the samples taken from atopic lesion. The AMCase gene expression was isolated in healthy and atopic skin regions.

Conclusion: The AMCase gene expression was isolated both skin regions. Our study shown that this gene is not only expressed stomach and lung and also expressed in skin.

Key words: Atopic dermatitis; chitin microparticle; chitin; chitinase.

Amaç: Bu çalışmada atopik dermatitli hastalardan alınan deri biyopsilerinde asidik memeli kitinaz (AMCase) gen ekspresyonu incelendi.

Hastalar ve yöntemler: Mayıs 2005 - Mayıs 2007 tarihleri arasında atopik dermatitli beş yetişkin hasta çalışmaya dahil edildi. Lezyonlu ve lezyonsuz bölgelerden deri biyopsileri alındı. Gerçek zamanlı polimeraz zincir reaksiyonu ile AMCase ekspresyonu incelendi. AMCase gen ürünleri, beta-aktin ile karşılaştırıldı.

Bulgular: Atopik lezyondan alınan numunelere kıyasla, AMCase yapımı derinin sağlıklı bölgelerinde daha yüksek oranda idi. Sağlıklı deri ve atopik deri dokusunda AMCase gen ekspresyonuna rastlandı.

Sonuç: AMCase gen ekspresyonu her iki deri bölgesinde izole edildi. Bulgularımız bu genin sadece mide ve akciğerde sınırlı olmadığını aynı zamanda deride de bulunduğunu göstermektedir.

Anahtar sözcükler: Atopik dermatit; kitin mikropartikülü; kitin; kitinaz.

Next to cellulose, chitin is the second most abundant glycopolymer in nature, and it is found in the walls of fungi, insects, parasitic nematodes, the cuticles of helminths, and the exoskeletons of arthropods. Chitinases are enzymes that degrade chitin. These enzymes are expressed by most lower organisms and are known to protect against chitin-containing pathogens. Chitinase genes have also been discovered within the mammalian genome and are known as the chitinase-like mammalian protein family. This family contains two functional chitinases: chitotriosidase, which is mainly expressed in neutrophils and macrophages, and acidic mammalian chitinase (AMCase), which is expressed in the lung epithelium, sinus mucosa, alveolar macrophages, and stomach of humans. Because most parasitic helminths synthesize chitin during several stages of their life cycle, chitinases are believed to play an effector role against parasites by binding to the chitin and mediating its breakdown. However, the high expression levels of chitinases in asthma and other inflammatory diseases suggests that this enzyme might have other roles beyond host protection.

Boot et al.[1] showed that AMCase is expressed in alveolar macrophages and the gastrointestinal tract, whereas chitotriosidase was only expressed in phagocytes. Zhu et al.[2] revealed that AMCase is expressed in the lungs of mice that have become sensitized to ovalbumin (OVA). In addition, they reported inhibition of AMCase due to allosamidin, reduced bronchial hyperreactivity, and decreased eosinophil counts and also demonstrated that anti-AMCase lowered the production of interleukin (IL)-13 in induced bronchoalveolar lavage (BAL).

Furthermore, Bierbaum et al.[3] found a strong correlation between a newly identified variant of AMCase (a single nucleotide polymorphism) and asthma severity, providing more evidence that AMCase might play a role in asthma pathogenesis. Increased expression of AMCase in cases of chronic rhinosinusitis with nasal polyps has also been reported, proving that AMCase expression is not limited only to the lungs and gastrointestinal tract as had been previously reported.[4]

Additionally, Shibata et al.[5] discovered that allergen-induced immunoglobin (Ig) E production and lung eosinophilia were downregulated when chitin was given orally, and this occurred both before and during allergen immunization. Similarly Strong et al.[6] showed that the intranasal application of chitin microparticles downregulates symptoms of hypersensitivity to Derp allergens and *Aspergillus fumigatus* in allergic mice models. Özdemir et al.[7] reported similar findings. They observed that treatment with chitin microparticles protect against lung histopathology in OVA-induced allergic mice models.

Therefore, most studies other than the one by Zhu et al.[2] indicate that it is possible that chitin, a natural inducer of chitinases, might offer protection against asthma, while it is clear that chitinases play important roles in allergic diseases, it remains to be seen whether these effects are protective or deleterious. In addition, further research is needed to determine the correlation between AMCase and other atopic diseases. Hence, in this study, we investigated AMCase gene expression in skin biopsies of atopic dermatitis patients in an attempt to bring further clarity to this issue.

PATIENTS AND METHODS

Five adult patients with atopic dermatitis were enrolled in this study in which skin biopsies were taken from lesional and nonaffected areas after obtaining the signed informed consent of each participant. In addition, this study was approved by the ethics committee of the Akdeniz University Medical Faculty.

The total ribonucleic acid (RNA) was isolated from the skin samples, and the levels of AMCase gene expression were tested by real-time polymerase chain reaction (PCR) using the QuantiFast SYBR Green PCR Kit (Qiagen, Hilden, Germany). They were then normalized and compared with the beta (β)-actin gene. The PCR primer sequences are given in Table 1.

RESULTS

Although AMCase expression was detectable in both the affected and unaffected regions of the skin, the expression level was significantly higher in the unaffected regions in all of the cases (Figure 1). We were not able to obtain informed consent from any pediatric patients or from those in the early stages of atopic dermatitis, so all of the patients were in the chronic phase.

DISCUSSION

Previous studies clearly showed AMCase expression in the stomach and lung tissues,[1] but our results indicated that this enzyme is also expressed in both the affected and unaffected dermal regions of atopic dermatitis patients. We believe that when inflammation occurred, AMCase consumption took place, leading to lower expression. Furthermore, in contrast to the study by Zhu et al.,[2] our data suggests that AMCase may have a protective role in allergic inflammation, as Reese et al.[8] showed when they found that pretreating chitin with AMCase decreased its capacity to trigger eosinophilia and allergic inflammation. In addition, they reported that AMCase-overexpressing mice do not show signs of

TABLE 1

Primer sequence

Gene	Forward sequence	Backward sequence
AMCase (Accession number: NM_201653.1)	CTA CTC CTG AGA ACC GCC	CCT GCT CAA AAG CTT CAC GC
β-actin (Accession number: NC_000007)	GGA TGA TGA TAT CGC CGC G	CCA TGC CCA CCA TCA CGC

AMCase: Acidic mammalian chitinase; β-actin: Beta-actin.

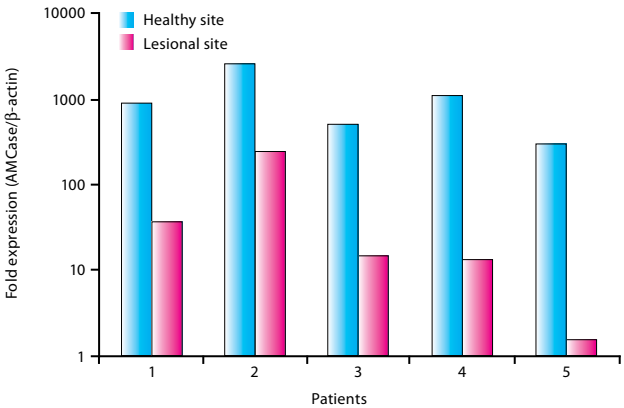

Figure 1. AMCase expression in the dermis of atopic dermatitis patients [Given as fold expression (AMCase/β-actin)].

inflammation and are even more resistant to a chitin-induced inflammatory reaction. Moreover, increased expression of AMCase in chronic rhinosinusitis with nasal polyps has been previously reported by Ramanathan et al.[4] Our results agree with this study which showed that the expression of this enyzme is not limited to just the stomach and lung tissues. Since the immunological profile changes during atopic dermatitis according to the phase of the disorder, longitudinal studies on chitinase activity in pediatric cases would be beneficial for understanding the role it plays in this disease.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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